INFANT FEEDING, HEALTH BEHAVIOR AND HOSPITALIZATION: A CASE-CONTROL STUDY

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A Thesis Submitted to the Yale University School of Medicine in Partial Fulfillment of the Requirement for the Degree of Doctor of Medicine, 1981.

Cynthia B. Aten

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DEDICATION

For my father, George A. Batte, Jr., whose generous support of my interrupted pursuit of a career in medicine has made it possible for me to do this work not heroically, but sanely.

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ABSTRACT

Most clinical and epidemiological studies in developing and industrialized countries have shown that breast-fed infants have a lower incidence of infectious illness, including illness serious enough to require hospitalization. Problems with studies of the relationship between breast-feeding and infectious illness include failure to define feeding categories and inadequate study design (such as failure to use a suitable control group). These shortcomings have led to failure to consider confounding variables and to study results that are contradictory. This case-control study of hospitalized infants was designed to eliminate these inadequacies.

The present study investigated 92 infants hospitalized with an infectious illness within the first three months of life at Yale-New Haven Hospital and 92 control infants matched for date of birth, sex, race, billing method and site of health care. The study used a chart review for all subjects and a telephone interview of mothers of infants cared for by private physicians to gather information about socio-demographic variables and about health attitudes and behaviors.

Results showed that breast-feeding was protective against illness requiring hospitalization in the first three months of life for infants from the upper social classes, particularly those whose mothers had a high health awareness. There were no significant differences between breast- and bottle-fed infants in respiratory illness, meningitis or

proven bacterial illness, but three times as many bottle-fed infants had illnesses involving the gastrointestinal tract. Accumulation of a larger interview sample will permit delineation of the relative effects on risk of illness of breast-feeding, socioeconomic status, maternal health behavior and smoking in the household.

INTRODUCTION

Studies spanning the entire twentieth century have investigated the relationship between mode of infant feeding, whether breast or bottle, and infant morbidity and mortality. Most often, these studies have shown that breast-fed infants have a decreased frequency of illness and death compared to infants who are not breast-fed (variously referred to as "formula-fed," "bottle-fed," or artificially fed"). Possible mechanisms of clinical protection have recently been investigated in in vitro studies that have revealed a host of potentially immunologically active elements in breast milk. Clinical studies in developing countries have shown a striking advantage for the breast-fed infant, particularly in terms of mortality. However, these studies often have been performed without benefit of scientifically prepared proprietary formulas, and the findings may not be relevant to industrialized countries.

This study, therefore, was conducted to determine whether breast-feeding protects infants less than three months of age from illnesses serious enough to require hospitalization. Because hospitalization of of infants occurs rarely, a case-control study design employing chart review was utilized. In addition, mothers of infants cared for by a private physician were interviewed by telephone to gather information about their health attitudes and behavior. This information permitted an analysis of the relationship of infant feeding, infectious illness and health behavior to determine whether the protective effect of

breast-feeding was due to breast milk *per se* or whether breast-feeding was part of a larger context which contributed to the maintenance of infant health.

BACKGROUND

A serious infection has the potential for being a devastating event in the life of a very young infant. Fortunately, in industrialized countries, improved living standards, alertness to signs of illness in the infant, and availability of potent antibiotics have dramatically reduced infant morbidity and mortality from infectious illness. Nevertheless, investigations of the relationship between illness and mode of infant feeding have continued to observe that morbidity and even mortality from infectious illness remains higher in babies who are not breast-fed than in those who are. Studies from several stances have been undertaken to elucidate the role that mode of feeding might play in infant morbidity and mortality. This section will describe three avenues of investigation:

1) laboratory research that demonstrates the presence and function of antimicrobial elements in breast milk which generally are not present, or are present in different concentrations, in the food received by non-breast-fed infants;
2) epidemiological and clinical studies in developing countries;
3) epidemiological and clinical studies in industrialized countries.

1. Laboratory Research

Human milk, in contrast to processed cow's milk preparations, is a live secretion with active enzymes, hormones, immunoglobulins, and

functional cells (Jelliffe 1971). The anti-infective components of breast milk can be considered in four general categories, as suggested by Fleischman and Finberg (1979):

a) the immunoglobulins

b) the cellular elements

c) the non-specific proteins and other macromolecules

d) specific Lactobacillus growth-enhancing factors.

Activity of many of these components has thus far been demonstrated only in vitro, and the clinical significance of their presence in breast milk has not yet been delineated (Butler 1979).

a) Immunoglobulins

Studies cited by Butler (1979) indicate that the fetus is able to produce IgM, IgG, IgD and possibly IgA. Also, in humans, maternal IgG is transported to the infant's serum via selective and active absorption by epithelial cells of the placenta. The maternally acquired systemic protection is important, as infants with hypogammaglobulinemia and X-linked agammaglobulinemia usually do not contract infections until levels of maternally acquired antibody begin to fall (Gerrard 1974). Reports regarding absorption of colostral antibody in the human have been conflicting, though most recent data do show some absorption of colostral antibody, but for only a very short period after birth (Ogra 1977).

However, of major interest is the long-term passive protective role played by the secretory IgA produced by B lymphocytes in the mammary

gland. (Although IgG, IgM and IgD are also present, IgA is found in by far the greatest amount) (Mata 1971). Maternal gut-stimulated lymphoblasts appear to migrate to the breast, where they then secrete specific IgA (Goldblum 1975); it is via this enteromammary circulation that antibodies to specific pathogens in the maternal-infant environment are made available to the infant. Concentration of antibodies is highest in colostrum at birth and declines dramatically over the next four days of life; the mammary gland, however, maintains a remarkable ability to produce large quantities of secretory IgA. Contrary to previous studies, which indicated that breast milk stimulated the neonate to increase its own production of IgA, a recent report by Gross and Buckley (1980) demonstrates no accelerated production of gastrointestinal IgA in the breast-fed newborn. Rather, when saliva samples were obtained four hours after feeding to avoid contamination by maternal milk IgA, salivary IgA remained low in both breast- and bottle-fed infants for the first fourteen days of life, with gradually increasing concentrations thereafter.

The secretory component added to the IgA by breast epithelial cells appears to play a role both in the secretion of IgA and in its protection against enzymatic degradation in the infant intestine. For example, this secretory component may contribute to the observation by Kenny *et al* (1967) that breast milk antibodies (primarily IgA) to *E. coli* are able to undergo gastrointestinal transit without significant change.

This is important because IgA apparently acts within the gut lumen. It appears to interfere with adherence of bacteria to mucosal cells, possibly by coating the bacteria (Butler 1979), which prevents colonization (Welsh 1979).

Antibodies specific to both bacteria and viruses have been detected in breast milk and include antibodies to E. coli, C. tetani, C. diphtheriae, S. pneumoniae, Salmonella, Shigella, and polio, coxsackie, ECHO, rota, respiratory syncytial and influenza viruses. As a specific example, Michael et al (1971) found that suppression of coliform flora in breast-fed infants correlated directly with the titer of colostral antibodies against E. coli, and as the concentration of immunoglobulins decreased during the four days postpartum, the number of coliforms increased. Suppression of coliforms was positively correlated with the presence of agglutinating and bactericidal activity against strains of E. coli in saline extracts of stool.

b) Cellular elements

T and B lymphocytes, macrophages, and polymorphonuclear neutrophils are all present in breast milk and are particularly abundant in colostrum. The functional mechanisms of these leukocytes in protecting the infant's gastrointestinal tract are not yet well-defined. Work by Pittard et al (1977) suggests that the breast milk macrophage may store and transport IgA produced by B lymphocytes. The macrophages and neutrophils are known to phagocytize staphylococci, E. coli and Candida albicans in vitro (Welsh 1979). These living cells are destroyed by pasteurization,

boiling and freezing. The significance of this loss can be suggested by Pitt's (1977) *in vivo* experiments using a model of necrotizing enterocolitis. Newborn rats made hypoxic and then given *Klebsiella* orally died unless they were nursed or given fresh rat milk. Frozen rat milk was not protective. Interestingly, washed colostral leukocytes restored protectiveness to cell-free milk. Jelliffe and others report that NEC is a rare disease in infants fed fresh breast milk, though some investigators refute this claim (Jelliffe, 1971; Kliegman, 1979; Barlow, 1974).

c) Non-specific proteins and other macromolecules

In this category are a number of breast milk components that have been studied extensively *in vitro*.

Lactoferrin is an iron-binding protein known to be synthesized by neutrophils (Butler 1979). By itself lactoferrin exhibits only a slight inhibitory effect against *E. coli* because *E. coli* produces its own iron chelator to maintain a constant iron supply. However, it is strongly bacteriostatic in the presence of antibody and bicarbonate (Welsh 1979). This bacteriostatic effect is eliminated by saturation of the lactoferrin with iron or by binding iron into a citrate-iron complex with the addition of citrate, both of which make free ferric ions available for bacterial metabolism (Klaus 1980). Kirkpatrick *et al* (1971) have also demonstrated inhibition of *Candida albicans* by unsaturated lactoferrin.

Lysozyme, which splits the peptidoglycans of bacteria, is found in human milk at a concentration 3000 times that in cow's milk and is

in a demonstrably more stable form. It acts *in vitro* with IgA to cause lysis of *E. coli* (Welsh 1979),*Enterobacteriacae* and gram-positive bacteria. Stool content of lysozyme is higher in breast-fed infants than in those fed cow's milk formula.

A lactoperoxidase system (which includes lactoperoxidase, thiocyanate and peroxide) also forms a component of the bactericidal activity in milk. The level of activity in human milk is about twenty times lower than in cow's milk, but it is more stable to gastric digestion (Welsh 1979). Activity of the system against streptococci, pseudomonas, *E. coli* and *S. typhimurium* has been demonstrated.

Also described is an anti-staphylococcus factor which inhibits the growth of these bacteria and is non-dialyzable, thermostable, and probably contained within the free fatty acid fraction of milk.

C3 and C4 components of complement have also been described in breast milk. C3 in particular may act to lyse bacteria in combination with specific IgA.

In addition to the specific antibody to viruses mentioned above, free unsaturated fatty acids and monoglycerides contained in the cream fraction of breast milk have been demonstrated *in vitro* and *in vivo* to possess nonspecific activity against a number of enveloped viruses, including herpes simplex, influenza, dengue and murine leukemia virus (Welsh 1979). Other non-immunoglobulin macromolecules have been demonstrated to be active against vesicular stomatitis (a relatively heat-stable molecule in the non-fatty portion of milk) (Matthews 1976), herpes simplex and rotavirus.

B lymphocytes in milk are capable of being stimulated to produce interferon, but because of the requirement for stimulation before synthesis, interferon cannot provide immediate protection. However, it is not clear at present whether interferon is in fact produced in the infant's gastrointestinal tract or whether it plays a protective role.

d) Specific Lactobacillus growth-promoting factor (bifidus factor)

Several studies have documented that intestinal flora in the exclusively breast-fed infant is dominated by Lactobacillus bifidus, an anaerobic gram-positive bacillus. Its predominance is enhanced by a carbohydrate growth-promoting factor, and probably by the high lactose concentration, low protein content and low buffering capacity of human milk. The metabolism of the lactobacillus produces large amounts of lactic and acetic acids, lowering the pH of the stool and thereby discouraging the growth of enteric pathogens such as pathogenic E. coli, shigella, salmonella and intestinal protozoa (Mata, 1971; Gerrard 1974). Exact mechanisms have not been established.

As can be seen from the above discussion, many anti-microbial elements have been identified in breast milk and found to be active in vitro. Although the activity in vivo of a few components has been demonstrated, precise mechanisms and clinical significance are not yet clear for most.

2. Epidemiological and Clinical Studies in Developing Countries

A second approach to studying the effect of mode of feeding on infant health is to examine data from developing countries. All studies

performed in locales where poverty is omnipresent and hygiene is poor demonstrate that breast-fed infants are less likely to suffer morbidity and mortality from infectious illness than are artificially fed infants. The following studies from Guatemala, Israel, Chile and India illustrate this general finding.

Mata's (1971) work with Guatemalan village neonates has shown a low rate of diarrheal disease during exclusive breast-feeding in the early months of life. As weaning progresses, attack rates increase and peak near the time of cessation of breast-feeding. Breast-fed infants in this population have a greater resistance to shigella during the time of exclusive breastfeeding.

Kanaaneh (1972) found a marked increase in the incidence of diarrhea serious enough to require hospitalization during the first six months of life in non-exclusively breast-fed infants in three Arabic villages in Israel.

A World Health Organization study (Plank 1973) of rural Chilean infants demonstrated a three-fold increased risk of postneonatal death among infants begun on bottle-feeding during the first three months of life as compared to infants exclusively breast-fed during those three months. The bottle-fed group, however, included low birth weight, high risk infants who were likely to be more susceptible to infection.

A recent study by Narayanan et al (1980) was undertaken in New Delhi, India, among low birth weight babies who were born to women of

low socioeconomic and educational status and who were at high risk for infection: these mothers had infections, premature rupture of the membranes for greater than 24 hours, or an unhygienic vaginal exam by a traditional birth attendent. Significantly fewer infants in the group given freshly expressed breast milk from 9 a.m. to 9 p.m. with milk formula at night developed infections compared to those in a similar group fed only with milk formula. Differences were greater for some of the major infections involving bacteria, but numbers were too small to draw conclusions.

In one of the better designed prospective studies, Chandra (1979) followed 35 infants living in India who were exclusively breast-fed for at least the first two months of life with a comparison group of 35 controls (matched for socioeconomic status, parental education, occupation, and family size) fed on fresh cow's or buffalo's milk. During the first twelve months of life, the breast-fed infants had a lower incidence of respiratory infection, otitis media and diarrhea.

These studies indicate that in developing countries, breast-fed babies have decreased morbidity and mortality from infectious disease, particularly that of a diarrheal nature.

There is no doubt that breast-feeding is associated with decreased morbidity and mortality, but the data do not necessarily support the claim of some investigators that the advantage offered is due to breast milk's anti-infective properties per se. Rather, better outcomes in breast-fed infants may also be significantly influenced by the following factors which make artificial feeding a perilous venture for infants in developing countries:

1) Malnutrition is a common problem in non-breast-fed infants due to over-dilution of expensive commercially available formula or due to the inadequacy of foods available for bottle-feeding (such as the feeding made of corn gruel in water plus a little cow's milk when available, as noted by Edwards in rural Guatemala).

2) The absence of facilities for adequately cleaning and storing formula and feeding supplies and the use of contaminated water may result in exposure to bacterial pathogens.

3) Perhaps breast milk simply is an adequate means of oral repletion for a child mildly to moderately affected by a diarrheal illness, and so physician-noted morbidity and mortality are favorably affected.

4) Perhaps also the closer mother-infant relationship in a breast-feeding pair leads to an enhanced sense of well-being in the couple which creates a survival advantage for the infant.

3. Epidemiological and Clinical Studies in Industrialized Countries

Studies in industrialized countries have spanned the twentieth century, and in general have supported the idea that breast-feeding is protective against illness and possibly against illness severe enough to require hospitalization.

At least as early as 1913, when Davis reported a study of morbidity and mortality in breast- and bottle-fed infants in Boston, American physicians were upholding the superiority of breast-feeding for infants. In 1922, Woodbury published an extensive statistical analysis based on data for 22,422 liveborn infants from eight cities in Massachusetts,

Connecticut, New Hampshire, Maryland, Pennsylvania, Ohio and Michigan. His analysis utilized "comparison of the deaths of infants receiving each type of feeding with the time lived by infants while receiving the same type of feeding." Infants were sorted into three feeding groups: exclusively breast-fed, both breast and artificially fed, and exclusively artificially fed. Mortality rates for artificially fed infants were three to six times higher than for breast-fed infants, depending on the month of life. Mortality rates for babies fed by both breast and bottle were intermediate. The advantage for breast-fed infants disappeared in the ninth month in comparison with the group fed by both breast and bottle. Woodbury observed a cumulative effect of mode of feeding on the mortality rate: the rate was higher the longer the period of previous artificial feeding and lower the longer the period of previous breast-feeding. The excess mortality among the artificially fed infants persisted even when multiple births, premature births and infants whose mother died within the first year were excluded from analysis. Taking into account race and nationality groups did not substantially alter the findings. Relative excess mortality in artificially fed infants compared to breast-fed infants in the same income group was significantly higher in the lowest paternal income group than in the highest paternal income group (ratios of expected deaths to actual deaths of 6.3 and 4.1, respectively).

To evaluate the merits of artificial formulas which many physicians saw as adequate replacements for breast milk in the 1920's, Grulee et al (1934) examined the incidence of infection in 20,061 breast- and artificially-fed indigent infants under the care of the Infant Welfare Society of Chicago during 1924-1929. Children were breast-fed for ten months if possible; if not, infants were fed diluted boiled cow's milk plus cane sugar, and received orange juice, cod liver oil, cereals and vegetables added in a predetermined way. Morbidity from gastrointestinal, respiratory and unclassified infections was lowest in the exclusively breast-fed group. Mortality among these 20,000 infants followed the same pattern, with even more striking differences: 66% of the total mortality was in 8.5% of the infants, those exclusively non-breast-fed. However, Grulee et al do not examine why these 8.5% of babies were not breast-fed, when breast-feeding was the normative behavior. Were their mothers ill, for example with tuberculosis, or were the infants themselves not doing well at birth and therefore more likely to develop life-threatening illnesses?

Discussants of this paper raised objections to the findings. One attributed the increased morbidity and mortality among artificially fed infants to lack of intelligence among indigent people, which made them unable to carry out such feeding properly, and to larger family size, which would decrease the amount of time available for infant care. Others cited decreased mortality in a certain large

Berlin orphanage compared with twenty years earlier, even though wet nurses had been discontinued during this time.

In a follow-up article, Grulee et al (1935) noted a rise in morbidity from respiratory disturbances and miscellaneous infections during the first five months of life for all groups; morbidity then decreased in breast-fed and partially breast-fed infants but continued to rise in the artificially fed infant. Gastrointestinal morbidity was practically non-existent for the breast-fed child. Mortality was markedly increased in the artificially fed infant for all three kinds of disturbances. In addition, mortality existed for the breast-fed infant almost entirely in the first two months of life.

In a later study, Robinson (1951), analyzing data from her Liverpool infant welfare clinic, found that infant morbidity and mortality for respiratory infections, gastroenteritis, otitis media, mastoid infection, infectious fevers and unclassified infections were affected by a number of factors. These were:

1) size of family (greater morbidity and mortality the larger the family);
2) mode of feeding (reduced in breast-fed infants);
3) prompt medical attention for illness (though percentage of breast-fed infants was the same in all social groups, morbidity was slightly higher in the lower class, laborer, than in the highest class in the study, clerk, but mortality was lowest in families of clerks and unemployed fathers, whose families were entitled to free medical care and were therefore seen promptly.)

The preceding studies have indicated a distinct advantage in morbidity and mortality for the breast-fed infant. Two studies conducted prior to the 1960's do not support this general finding.

Norval (1949) studied infants born in Rochester, Minnesota, from 1944-1946, and seen every month during the first year of life in a city-wide system of well-child clinics which served most of the population. She did not include infants who died before the end of the first year of life or infants who were chronically ill. Data from 417 babies with 679 illnesses were analyzed. Norval found a steady rise in the number of illnesses from all causes as infants approached their first birthdays. When compared to the first six months, the last six months of the first year showed three times the number of illnesses from all causes, as well as from gastrointestinal and respiratory illness. Of particular interest is her finding that breast-fed babies had a significantly higher illness rate (1.69 ± 0.07 per infant) than babies never breast-fed at any time (1.16 ± 0.16 per infant). This increased incidence of illness was noted only during the second six months of life. Respiratory illness followed a similar pattern.

Norval noted that her findings were in direct opposition to those of Stevenson (1947), whose Boston study of 263 infants found no significant difference in the number of respiratory infections per infant in the first six months of life. However, he found a decreased number of respiratory infections per breast-fed infant in the second six months.

Norval did acknowledge that other factors, such as the diet of the mothers during breast-feeding, exposure to older children and adults, and housing conditions "may obliterate the influence of breast-feeding." In her study, breast-feeding was not defined: groupings were established according to the duration of breast-feeding, but it is not clear whether this is exclusive breast-feeding or whether supplementary foods are being given in addition to breast milk. No attempt was made to analyze for the effect of demographic factors or socioeconomic status on the data.

A carefully performed prospective study (1953-1957, published 1959) of 402 infants in two areas of Norbotten, Sweden, had as one of its objectives to establish the incidence of infection in different feeding groups. These groups were defined as follows:

I exclusive breast-feeding 0-2 weeks

II exclusive breast-feeding 1-2½ months

III exclusive breast-feeding 3-6 months

IV exclusive breast-feeding 6½ months or longer

The only difference between the groups was a significantly higher number of school-age siblings in group IV. Declared yearly incomes varied among the groups and were lowest in group IV, but were not felt to be indicative of the actual standard of living due to the existence of a partially non-cash economy. The incidence of epidemic disease (measles, varicella, rubella and roseola) was found to be low, with no significant difference among the groups. A higher incidence of acute upper respiratory and gastrointestinal illness

(rhinitis, cough, otitis media, URI with pyrexia,and acute diarrhea) was found in the rural area of study, which had poorer housing conditions.

The investigators found that the frequency of some acute infections (cough and otitis media) was higher in the early-weaned groups than in the late-weaned group, but the difference was not statistically significant. However, if all types of infection were grouped together, the earliest weaned group showed a significantly higher over-all incidence of infection than the late-weaned group ($0.001 < p \leq 0.01$). This study does, therefore, follow the general trend of the literature, but its investigators downplay any observed differences as being never more than "probably significant" ($p = 0.05$) except when they grouped all infections and considered an average incidence of all types.

One difficulty with the study, according to the investigators, was the incomplete data on a large group of infants who therefore could not be included in the analysis, an omission which could influence the results.

The preceding studies not withstanding, declines in the prevalence of breast-feeding and in infant mortality during the 1920's to 1960's paralleled each other. Physicians began to feel that mode of feeding, given the introduction of proprietary formulas and improved refrigeration, was of little consequence in infant morbidity and mortality. However, with a resurgence of interest in breast-feeding came renewed attempts

to assess the clinical impression that breast-fed babies suffered fewer illnesses, particularly of the gastrointestinal and respiratory tracts. Although studies since the 1960's have continued to show an advantage for the breast-fed infant, two studies contradict this trend.

Adebonojo's study (1971) is of interest in that he found no differences between breast-fed and bottle-fed infants in a suburban residential practice when he looked at episodes of illness (fever, respiratory and gastrointestinal) during the first year of life, but he did not use statistical methods to analyze his data. In addition, his categories for feeding were not well-defined. For example, he classified as breast-fed infants who were fed "primarily" at the breast for the first three months of life.

The second conflicting study comes from the Research Sub-committee of the South-East England Faculty of the Royal College of General Practitioners (1972). It examines the incidence of infectious illness during the first year of life in 334 infants residing in an area where the standard of living in general was stated to be high (though no attempt was made to control for socioeconomic status). Infants were grouped according to mode of feeding; breast-fed infants included both totally and partially breast-fed. The incidence of infectious illness in the entire group of breast-fed infants was then compared with the incidence in the exclusively bottle-fed group. Any differences between the two groups favored

the breast-fed infant, but nowhere were the differences significant according to the chosen level of significance.

Again, the finding is not of a disadvantage for breast-fed babies (as in Norval's study), but of a lack of advantage in terms of morbidity.

In contrast to these two studies, several studies of incidence of illness in breast- and bottle-fed infants in the 1970's and early 1980's continue to show an advantage for the breast-fed infant.

In an interesting retrospective study utilizing detailed information from hospital feeding records, Winberg and Wessner (1971) in Stockholm compared breast milk consumption in days one to five of life in infants with onset of probable hematogenous infection on days four to ten of life as compared to matched controls. Cases showed a significantly lower breast milk consumption during the first five days of life. The investigators attributed this lower intake to lower milk production by the mother, since 1) case infants were as able as controls to empty the breast, and 2) the symptomatic period for the case infants was not included in analysis of the feeding data. This decreased intake of breast milk by infants who later developed septicemia was felt by the investigators to suggest that colostrum and early breast milk offers protection against coliform septicemia in the neonate, and the more breast milk the better. However, the decreased intake by the case infants may

represent the earliest symptom of illness, since in breast-feeding, supply is usually closely related to demand.

In an urban Canadian community, Chandra (1979) prospectively followed for 24 months a group of 30 exclusively breast-fed infants and 30 controls fed a cow's milk formula who were matched for socio-economic status, parental education and family size. He found a significant reduction in respiratory infection and otitis media ($p < 0.001$) in the breast-fed group, and a less dramatic reduction in diarrhea ($p < 0.01$). His numbers are small, and though his period of follow-up was 24 months, only two months of exclusive breast-feeding were required for inclusion in the breast-fed group.

Cunningham (1977, 1979), in a study of 503 infants seen regularly at a pediatric clinic in a small town, rural setting in New York State, found breast-feeding to be consistently associated with decreased morbidity, independent of lower educational level, lower maternal age, presence of older siblings, low birth weight and male sex, which in themselves are associated with increased morbidity. Decreased morbidity was also apparent in episodes of significant illness (defined as otitis media, lower respiratory illness, vomiting or diarrhea, and any illness requiring hospital admission, excluding trauma or surgery for congenital anomalies) among families with the highest paternal educational level: 62 per 100 infants in the breast-fed, 91 per 100 in those receiving limited breast-feeding, and 126 per 100 in the artificially fed. Differences in morbidity between breast-fed and artificially fed infants were 16-fold in the first

two months, fourfold in the first four months, and nearly twofold in the first year. The apparent protection offered by breast-feeding was found not to be an artifact of different exposures to child care arrangements or to maternal smoking. Cunningham found that despite 40% of aggregate patient-weeks being spent in breast-feeding during the first four months of life, only 4% of the hospitalizations during this time (1 of 23) were of breast-fed infants, a highly significant difference ($p < 0.001$). He concluded that the protection offered by breast-feeding is more striking against serious illnesses than common ones, and is especially evident in the early months of life. However, the number of hospitalized infants in the study is too small to merit definitive conclusions.

Cunningham's category of "breast-fed" was defined as breast-feeding beyond 4½ months of age, without further delineation of time of introduction, type or amount of supplementary food. The category of "artificially fed" included infants who were weaned less than six weeks after birth as well as those fed only formula from birth. The latter definition might actually serve to decrease differences in respiratory morbidity if Downham's (1976) and Pullan's (1980) observation that early breast-feeding appears to offer enduring protection against respiratory syncytial virus infection is accurate. Their work is discussed below.

In addition to general studies examining the relationship of mode of feeding to incidence of different kinds of infectious

illness, some studies have focused on a particular type of illness, such as gastrointestinal or respiratory.

For more than thirty years, researchers have found breast-fed infants to be at a lower risk for diarrheal disease, though often this observation was made incidentally (Alexander, 1948; Hinton, 1958; Ironside, 1970).

Of 107 infants with acute gastroenteritis admitted during a three-year period to the Kaiser-Permanente Medical Center of Hayward, California (Larsen, 1978), only one baby was being breast-fed at the time of admission. A concomitant survey of a 10% sample of mothers nursing at birth in the Kaiser-Permanente population showed that the incidence of acute gastroenteritis in breast-fed infants was much lower than predicted and was statistically significant. The authors concluded that breast-feeding was protective against gastroenteritis serious enough to require hospitalization. In this study, a random-sample survey of breast-feeding prevalence was used rather than a matched control population. The authors felt that sampling errors could not have been large enough to affect their conclusions, because of the very large difference between expected and actual hospitalizations of breast-fed infants.

France et al (1980) found that breast-fed infants, including those partially supplemented wirh formula, have a significantly lower incidence of salmonella infection. During the two-year

period of their study in Arkansas, 253 cases of salmonella infection in infants less than one year of age were reported. Twelve of these infants had been breast-fed sometime during the first year of life but had discontinued breast-feeding an average of four months prior to infection. The incidence of reported salmonella infection in breast-fed infants was therefore zero per 1000 in the clinic population and 0.05 in the private population, as compared to 14.3 and 3.8 in the bottle-fed clinic and private populations. Some reporting bias is likely to be operative here, but the authors feel it cannot account for the magnitude of the difference.

Similar findings have been reported in studies of respiratory infection. Downham et al (1976) established that breast-fed infants have a lower prevalence of respiratory syncytial virus (RSV) infection requiring hospitalization by comparing a group of infants admitted to hospital with RSV infection with unmatched controls generated in waiting rooms of Newcastle city child health clinics. Eight of 115 cases had been breast-fed (none continuing to the time of admission), compared to 46 breast-fed of 167 controls, some for as little as one month or less. The effect of breast-feeding seemed to be independent of social class for classes I, II and III, but not for IV, V and other (primarily unemployed), though the numbers here were small. Concomitant laboratory studies revealed that RSV neutralizing activity in colostrum correlated most closely

with the titer of specific IgA antibody in the colostrum, thereby designating specific IgA antibody as the protective agent against RSV.

In a similarly designed study, Pullan et al (1980) compared feeding histories on 127 infants hospitalized with RSV infection and 503 non-hospitalized age-matched controls. The odds ratio or approximate relative risk of not being breast-fed was 2.2 with 95% confidence limits of 1.4 and 3.5, which indicated that non-breast-fed infants had an increased risk of being hospitalized for RSV infection. When adverse factors such as "mother's care poor," "single mother,""another child sleeping with baby," "gestation less than 36 weeks," "mother smokes," etc. were controlled for separately and the prevalence of not breast-feeding was examined, the relative risk fell slightly but remained greater than 2.0. Because more severely ill infants (as indicated by requirement of tube feeding or IV fluids) did not have an increased risk of admission compared to less severely ill infants, bias attributable to possible physician reluctance to hospitalize a breast-fed baby was eliminated as an explanation for the difference in relative risk of admission for breast-fed and non-breast-fed infants. Home health visitors obtained the epidemiologic information and scored the mothers on their care of their infants. Breast-feeding was felt to influence their assessment of maternal care in a positive direction, but when only maternal care and breast-feeding were

considered statistically, the authors contend that breast-feeding remained significant. They therefore consider breast-feeding to be a factor independent of maternal care in influencing infection with RSV. Of interest is the finding, as in the preceding study, and in contrast to findings in studies of gastrointestinal illness, that breast-feeding seems to exert an enduring protective effect, possibly through colonization of the infant's nasopharynx by lymphocytes sensitized to RSV or through stimulation of the infant's own immune response.

Few studies have examined the effect of breast-feeding on illnesses severe enough to require hospitalization. Cunningham's number of hospitalized infants is small, and most other studies which include hospitalized infants are concerned with only one type of illness. A recent paper by Fallot et al (1980) in Syracuse addresses this relatively neglected area.

The authors claim that infants exclusively breast-fed for the first three months of life have a lower rate of presumed and documented infection ultimately requiring hospitalization. The prevalence of exclusive breast-feeding within their moderate sized urban community was determined for "clinic" and "private" populations by a chart review of consecutive patients; matched controls were not used. Hospital records of all infants 0-3 months of age admitted for suspected or confirmed infection were reviewed to determine the incidence of exclusive breast-feeding. By X^2 analysis,

a statistically significant under-representation of breast-fed infants among hospitalized infants was noted. Despite the marked differences in percentage of infants being breast-fed among the well population (13.5% in the clinic population; 38.0% in the private population), the clinic and private patients are then grouped together to produce an expected percentage of hospitalized infants who would be breast-fed if breast-feeding offered no advantage. Of note is the fact that, although 19.9% of the illnesses requiring hospitalization were bacterial infections, there were no culture proven bacterial infections in exclusively breast-fed infants.

A critical problem with this study is the failure to provide matched controls for the hospitalized cases. This deficit may lead to many kinds of inequalities in the groups being compared, and thus bias the results.

Problems with previous studies

As can be seen from the above discussion and critique of papers which span the twentieth century and include studies of a variety of infectious illnesses, of specific illnesses (gastrointestinal and respiratory), and of illnesses requiring hospitalization, it is no simple task to determine the relationship between breast-feeding and infectious illness.

Problems with this literature include the following:

1) The overall contention of the literature is that breast-feeding is protective against infectious illness, but a few studies have generated contradictory results. This can happen in case-control

studies, as Feinstein and Horwitz point out, when rigorous efforts to eliminate bias are not consistently undertaken. Other factors which might influence the risk of illness are inadequately considered.

2) Studies generally fail to define breast-feeding and other feeding categories, or they utilize such different feeding categories that comparison of results is meaningless.

Related to this problem are the different patterns of introduction of solid foods in breast-fed and formula-fed babies: bottle-fed infants often are fed solids and/or juices much sooner than breast-fed infants (Neumann, 1976). A survey by Ross Laboratories (Market Research Department, 1978) found that diarrheal episodes per infant in both breast- and bottle-fed infants receiving solid foods and/or juices were almost double those in both groups not receiving solids and/or juices. It is therefore important to have precise definitions of feeding categories to draw meaningful conclusions.

3) Most of the studies have looked at the occurrence of illness in general, and the small number of hospitalized infants generated in these investigations has been inadequate to allow conclusions about hospitalization.

4) The one study focusing on illnesses severe enough to require hospitalization failed to use a suitable control group.

In addition to the obvious methodological and numerical problems noted above, there are issues, best raised in a paper Sauls (1979), which make studies of the relationship between mode

of feeding and infant morbidity extremely problematical and subject to bias. Sauls cites two major problems in selecting comparable populations:

1) Infants cannot be randomly assigned to breast or bottle-feeding study groups, because mothers choose how to feed their infants, and studies have shown that there are differences between mothers who choose to breast-feed and those who choose bottle-feeding (Newton, 1971; Switzky, 1979). Because of the educational, socio-economic and demographic factors that make breast-feeding mothers different from bottle-feeding mothers, access to medical care and behavior toward the infant as well as the mother's ability to serve as the infant's primary health care provider are likely to be different in these two groups.

Feeding differences may also contribute to discrepancies between the groups in the frequency of disease entities. For example, Sauls notes the potential over- or under-reporting of diarrhea in the breast-fed infant, whose stools tend to be looser and more watery normally.

2) There is a one-way flow from the breast-fed to the bottle-fed group. That is, infants who are breast-fed may switch to bottle-feeding, but rarely is a bottle-fed child changed to the breast. Any deviation from the norm in the mother's or infant's health increases the likelihood of bottle-feeding, which tends to load the bottle-fed group with potentially less healthy babies.

Feinstein (1979) indicates additional difficulties in case-control studies, which is the design most often found in the breast-feeding/infant illness literature. He discusses potential bias that should be minimized in such studies. He contends that one cannot, in comparing a group with an outcome to a group without it, attribute statistical difference in outcome to a causal agent unless one is certain that "no major biases have occurred as the true or alternative causes of the observed differences;" that is, unless one is certain that there are no confounding variables.

It was Feinstein's analysis, supplemented by the methodological standards for case-control research discussed in Horwitz and Feinstein's paper (1979), that helped establish the framework for the present study design. This author sought as rigorously as possible to avoid the problems of previous studies as discussed above and to eliminate confounding variables. The implication of each confounding variable was considered as the answer to the central question was sought: does breast-feeding per se protect infants less than three months of age from illnesses severe enough to require hospitalization?

METHODS

A case-control design was used and data were collected from chart review and telephone interviews. Approval was obtained from the Human Investigations Committee of Yale University School of Medicine and Yale-New Haven Hospital before the study was begun.

Cases

Case infants were identified from a computer-generated list of all infants less than 90 days old admitted to Yale-New Haven Hospital from July 1, 1979 through June 30, 1980 (approximately 450 infants). To be included as a case required the following characteristics:

1) admitted for infectious or suspected infectious disease

2) born at Yale-New Haven Hospital (so that the investigators had access to birth records)

3) discharged with mother as a neonate (to eliminate children with serious and prolonged neonatal difficulties which might predispose to infectious illness)

4) without congenital anomalies that would directly affect mode of feeding.

Excluded from the cases were:

1) infants with an underlying disease which has an associated increased risk of infection, such as sickle cell disease or cystic fibrosis

2) infants of less than 37 weeks' gestation

3) infants admitted for failure to thrive regardless of reason.

Controls

Using another computer-generated list of all Yale-New Haven Hospital births between April 1, 1979 and June 30, 1980, the investigator generated for each of the case infants a control infant having the same characteristics as case infants:

1) born at Yale-New Haven Hospital

2) discharged with mother as a neonate

3) gestation of 37 weeks or more

4) without congenital anomaly that would directly affect mode of feeding

5) without perinatal complications that might have affected mode of feeding

6) without underlying disease associated with increased risk of infection, such as sickle cell disease or cystic fibrosis.

In addition, controls were not hospitalized within the first three months of life.

The control infants were matched for:

1) date of birth within 6 weeks

2) sex

3) race (Black, White, Hispanic)

4) billing method (Title XIX or private insurance)

5) site of pediatric care.

The control infant was located by identifying the infant nearest the case infant in date of birth who possessed the requisite matching criteria. The matching criteria were chosen to minimize demographic susceptibility bias with the following considerations in mind:

1) Date of birth. Infants born at about the same time would be exposed to seasonal pathogens at about the same age.

2) Sex. Studies have indicated a greater risk of illness and hospitalization for male infants.

3) Race. Similar studies have shown an increased risk of illness and hospitalization for non-white infants.

4) Billing method. Whether a family's hospital costs were paid by Title XIX or town welfare, or by some form of health insurance, including pre-paid health plans, was considered to be a rough indicator of socioeconomic status.

5) Site of health care. Clinic versus health plan or private physician was also felt to be a rough indicator of socioeconomic status. The main purpose of this matching criterion, however, was to minimize detection bias: the investigator felt that physicians in practice together would have similar responses to illness and similar threshholds for admitting a child to the hospital.

Special Considerations in Selection of Controls

1. In choosing for case infants seen at two neighborhood clinics (Fair Haven Clinic and Hill Health Center),controls were selected

from infants receiving care at the Yale-New Haven Hospital's Primary Care Center (PCC) because:

a) the author had ready access to the charts and therefore to the feeding histories of PCC children and felt that Hill Health Center and Fair Haven Clinic patients were likely to be difficult to reach by telephone; and

b) it was also felt that roughly the same population was served by the three clinics, and that an appropriate match could be generated using the other four criteria.

2. If a matched control whose birthdate was within 6 weeks of the case could not be found, the following was done:

1) Sex as a matching criterion was dropped, and an infant of the same race, billing method and site of health care but opposite sex was chosen. This was necessary in generating controls for several private patients and for several Hispanic patients.

2) Site of health care was dropped if the above maneuver did not produce a match. The investigator chose as a control the infant nearest the case in date of birth who matched in all other respects but was seen by any other private pediatrician.

In short, race and socioeconomic status were retained as matching criteria as often as possible.

Date Extraction: Chart Review

The hospital charts of all case and control infants were reviewed and the following information was extracted:

1) for cases: information relating to the hospital admission: discharge diagnosis, age on admission in days, dates of admission, significant findings during the hsopitalization, such as positive cultures

2) feeding history: birth, interim, and on admission (or at a comparable age for controls)

3) information about the infant's mother: date of birth, marital status, parity

4) information about the infant: mode of birth, birth weight, gestational age, Apgar scores at one and five minutes, neonatal difficulties

5) social information, if available in the chart: household members, parental employment, child care arrangements.

The data abstraction form may be found in the Appendix.

Case infants were grouped into the following diagnostic categories:

1) rule out sepsis
2) sepsis
3) meningitis (both bacterial and viral)
4) diarrhea
5) vomiting and diarrhea
6) abscess
7) respiratory (including otitis media)
8) other (including impetigo and conjunctivitis, staphylococcal cellulitis, rule out meningitis, probable viral syndrome, hypernatremic dehydration, and tussive episodes associated with choking and cyanosis)

If a child had multiple diagnoses, the primary diagnosis was the basis for classification.

Illnesses were further classified on the basis of etiology, as follows:

1) definite bacterial (culture proven)
2) definite viral (characteristic cerebrospinal fluid changes for viral meningitis, rise in viral titers, or positive viral cultures)
3) probable bacterial (otitis media and chlamydia pneumonia diagnosed on the basis of conjunctivitis since birth and a compatible chest x-ray)
4) probable viral (bronchiolitis and "rule out sepsis" cases with negative cultures of blood, urine and CSF)
5) cannot assign (diarrhea, vomiting, pneumonia)

Data Extraction: Telephone Interview

For cases and matched controls who were cared for by a health plan or private doctor, a 10-15 minute telephone interview with the infant's mother was conducted. The interviews took place from 7 to 18 months after the hospital admission, or comparable age for controls. The interview was conducted by one of two investigators (the author or Donna Torcia, a research assistant). To minimize potential bias introduced by an interviewer's preconceptions, the interview adhered to a highly structured format, with the same questions being asked of each participant and the answers being recorded in as uniform a way as possible.

The interview was conducted with the following purposes:

1) To review data about mode of feeding for the cases and to obtain a feeding history for the controls.

2) To obtain a more precise measure of socioeconomic status utilizing the Hollingshead Two Factor Index of Social Position (1957).

To employ this index, the occupation and education of the head of the household must be known. As customary, the father was considered to be household head for a married couple; the single, separated or divorced mother was considered to be head of her household.

3) To obtain information about variables which may be related to infectious illness, such as number and ages of other children in the household and regular exposure to other children through day care or babysitting arrangements.

4) To determine the mother's attitudes and behaviors related to health maintenance and promotion. This was done to attempt to take into account potential differences in the two groups of mothers.

Based on this information, a scoring system was developed for those questions related to infant health. This Child Health Index is as follows:

Question	Scoring
Had you decided how you would feed ____ before s/he was born?	No = 0 Yes = 1
What were the things you thought about as you decided?	Decided not to score because felt it would weight score in favor of breast-fed infant.
Did you attend childbirth classes before ____ was born?	No = 0 Yes or previous classes = 1
Did anyone in your household smoke when ____ was ____ old?	No = 4 Father = 1 Mother = 0
Do you have ipecac at home? Have you had to use it?	No = 0 Yes, but used = 1 Yes or child less than 10 months old = 2

Has ____ missed any appointments for regular check-ups in the past year? If yes, was the appointment rescheduled and kept?	None missed or rescheduled = 1 Missed appointment = 0
Is ____ up to date on his/her baby shots?	Yes = 1 No = 0
Did you use any sort of baby carrier, like a Snuggli (R), when ____ was a small baby?	Yes = 1 No = 0
Do you use a restraint system for ____ when s/he travels in a car?	Yes, always = 4 Yes, usually = 2 Yes, sometimes = 1 No = 0

Points given for each item were added to obtain the Child Health Index (range 0-15)

A similar scoring system for the questions directed at maternal attitudes and behavior yielded a Maternal Health Index:

Subject of question	Scoring
Smoking at time of interview	No = 2 Yes = 0
Personal use of seat belt	Yes = 2 No = 0
Most recent dental care	< 1 year = 0 > 1 year = 1
Most recent Pap smear	< 1½ year = 0 > 1½ year = 1
Weight when not pregnant	Yes, overweight = 0 Not overweight = 1
Limitation of salt intake	Always or usually = 2 Sometimes = 1 No = 0
Consumption of soft drinks/week	≤ 2 8-oz glasses = 1 > 2 8-oz glasses = 0

Consumption of refined sugar (as sweet desserts or snacks -- number/day	$\leq$ 3/week = 2 $>3 \leq 7$ = 1 >7 = 0
Consumption of caffeine (tea and coffee)/day	$\leq$ 2 cups = 2 $>$ 2 cups = 0
Regular exercise	None = 0 $\leq$ 2 times/week calisthenics = 1 $>$ 2 times/week calisthenics or aerobic $\leq$ 2 times/week = 2 aerobic $>$ 3 times/week = 3
Experience of stress and methods of coping	Decided not to score because it was difficult to distingu "good" coping mechanisms from "bad" on the basis of such a brief inquiry

Points given for each item were added to obtain the Maternal Health Index (range 0-17).

The complete questionnaire is included in the Appendix.

After conducting the telephone interview, each infant's feeding was categorized as follows:

1) exclusively formula-fed
2) exclusively breast-fed to time of admission for cases or to the comparable age for controlls -- included in this category are infants who took an occasional bottle of formula, less one per day
3) breast-fed plus regular daily intake of solid foods
4) breast-fed plus regular daily intake of formula -- these infants could also be receiving solid foods.

These categories were defined prior to analysis of the data.

Consent Procedures

Prior to initiating the telephone interviews, a letter was sent to all area pediatricians to acquaint them with the design and intent

of the study and to obtain their tacit approval and cooperation. Letters explaining the study and asking for participation were sent to those mothers of case and control infants whom the investigators intended to interview. Verbal agreement to participate was obtained at time of interview.

Statistical Analysis

All data from the chart review and interviews were then coded. Coding criteria can be found in the Appendix.

The data were analyzed using the chi-square method and t-test.

RESULTS

The study included 92 case infants and 92 control infants.

Matching Variables

As can be seen in Table 1, cases and controls were nearly identical in the matching variables: sex, race, billing method and site of health care. The slight differences, none of which approach statistical significance, are due to inability to find perfect matches for a small number of cases. Title XIX infants in the care of private pediatricians and Hispanic infants posed particular difficulties (3 cases and 2 cases, respectively).

Other Variables

Cases and controls were compared with respect to non-matching variables to determine the presence of differences between the two groups. Results are shown in Table 2.

There was no significant difference between cases and controls in the type of birth, Apgar scores, or neonatal separation. There were more teenage mothers ($\leq$ 19 years old) among the controls, which may contribute to the observations that more mothers of controls were single and had fewer pregnancies. These differences were not statistically significant. On three occasions the author substituted the next appropriate control when the first control could not be reached for interview; this probably accounts for the larger number of interviews obtained in the control population. The author concluded that cases and controls had equal demographic and clinical susceptibility.

Mode of Feeding: All Cases and Controls

Infants were grouped according to mode of feeding: (1) at discharge from the hospital as a newborn and (2) at the time of hospital admission (or at a comparable age for controls). Results are shown in Table 3. Differences between cases and controls are not significant ($p = .188$ at time of admission).

As shown in Table 4, when all infants receiving any breast milk were grouped together, breast-feeding at the age of admission occurred more frequently in the controls ($p = .036$).

To determine which factors might contribute to the significant difference between case and control infants in mode of feeding at the age of hospitalization, cases and controls were stratified into Title XIX or non-Title XIX infants. Table 5 shows the percentages of breast-fed infants in each group.

There was no significant difference between case and control infants in the Title XIX group at either time; however, the number of breast-fed infants in both cases and controls is very small. By contrast, in non-Title XIX infants, breast-feeding was more prevalent among controls, and this difference reaches statistical significance when all breast-fed infants are grouped (Table 6).

The stratification using site of health care (private doctor versus clinic) showed similar results.

Telephone Interview

Of infants cared for by private pediatricians, telephone interviews were completed with mothers of 79% of cases (34 of 43) and 93% of controls (40 of 43). The interview sample was no different in mode of feeding from the entire sample of infants cared for by private physicians (Table 7).

There were no significant differences between cases and controls surveyed by telephone in the following variables (for details, see Appendix: Interview and Coding Criteria):

A) General

1) marital status at time of interview
2) number of children at home
3) infectious illness in the household during age of interest

B) Infant-related health attitudes and behaviors

1) antenatal decision about feeding
2) reasons for feeding decision
3) postpartum change in feeding plans
4) prenatal education
5) day care
6) possession of ipecac
7) use of ipecac
8) missed check-ups
9) immunizations up to date
10) use of baby carrier
11) use of appropriate infant restraint in car

C) Mother-related health attitudes and behaviors

1) seatbelt use
2) dental care
3) Pap smear
4) overweight
5) soft-drink consumption
6) coffee consumption
7) regular exercise
8) stress

Three variables provided fruitful areas for investigation of differences between cases and controls: 1) social-demographic data, 2) several health behaviors, and 3) health indices. There were no major differences between cases and controls in social-demographic data; nevertheless, this was deemed an area worth further consideration. Significant differences between cases and controls were noted in several health behaviors, notably smoking, and in the health indices.

1) Social-demographic Data

At the telephone interviews, more detailed information about socioeconomic status (SES) was obtained. Educational status, work and SES are collapsed into 2 X 2 matrices in Table 8. Cases and controls are not significantly different from each other on these variables. However, concealed within this collapsed table are several differences between cases and controls. More controls than cases were in the upper divisions of the SES-related variables. For example, 5.9% of cases and 30.0% of controls had fathers with post-graduate education. This difference in education translated into a less marked difference in employment, with 11.8% of case fathers and 22.5% of control fathers in Hollingshead's highest category of employment. In addition, in the expanded SES table, classes II, III and IV were almost equal in content when cases were compared with controls for each class, but half as many cases as controls were in class I (11.8% of cases versus 22.5% of controls) and seven times as many cases were in class V (17.6% of cases versus 2.5% of controls): there were more very high SES controls and very low SES cases.

2) Health Behaviors

Three of the health behaviors assessed at the interview were different in cases and controls (Table 9). Of these, smoking was the most important.

Significantly more case households than control households had at least one cigarette smoking member. On further analysis, there was no difference between the two groups in mothers' smoking, but more case fathers were smokers, and twice as many case fathers smoked more than a pack per day.

In addition, more controls than cases showed healthy behavior by limiting their salt intake and using less refined sugar.

3) Health Indices

Although there were no differences between cases and controls on most health behaviors and attitudes, when the Child Health Index (CHI) and Maternal Health Index (MHI) were calculated, more cases than controls were noted to have a low score on both (Table 10). The difference was significant for the CHI ($p = .047$).

Stratifications

Because of the importance of SES and the differences between cases and controls in smoking and the health indices, the sample was stratified to investigate the effects of these variables.

When case and control infants were considered together, breast-feeding both at discharge and on admission was more prevalent with

well-educated mothers and fathers (Table 11) and social classes I and II.

To explore this in more detail, feedings were examined for cases and controls in each social class. The control group in social class I contained significantly more breast-fed infants than the case group, as can be seen in Table 12 ($p = .022$). Differences in other social classes were not significant.

There was no significant difference in mode of feeding between cases and controls in high or low maternal education groups or in high or low paternal education groups. However, when the stratification was done by SES, a difference was noted in the high SES group: there were significantly more breast-fed babies among controls in the families with high SES (Table 13).

When cases and controls were grouped together and the number of smokers in each feeding category was examined, a larger percentage of breast-fed infants belonged to non-smoking households and parents. Breast-feeding mothers were particularly likely to be non-smokers, and formula-feeders tended to be heavier smokers (Table 14).

When households were stratified into smoking and non-smoking, there was no significant difference in mode of feeding between cases and controls in either type of household (Table 15).

When cases and controls were stratified according to high and low CHI and MHI, there was no significant difference between cases

and controls in mode of feeding among low scorers on both indices (Tables 16 and 17). However, among the high scorers on both indices, significantly more control infants were being breast-fed at age of admission.

Relationship of SES to Smoking and Health Indices

Because social-demographic variables, particularly SES, seemed to be important, the author examined further the relationships of these variables to smoking and to the health indices.

Consumption of cigarettes was lower among the more highly educated parents. More mothers with high educational status were non-smokers, and only 4.5% of more highly educated mothers smoked a pack or more per day, compared to 36.7% of less well-educated mothers (Table 18). More well-educated fathers were also non-smokers, but an equal percentage (approximately 30%) of fathers in the two education categories were reported to consume a pack or more per day.

Households in the upper social classes were predominantly non-smoking; lower SES households were predominantly smoking (Table 19).

When families were stratified according to high and low SES, there was no significant difference between cases and controls in CHI (Table 20). However, significantly more high SES controls had a high MHI: in the presence of high SES, a high maternal health awareness was protective.

Mode of Feeding: Diagnosis and Etiology in Cases

The study was also designed to determine whether there were differences in the types of illness in breast-fed and formula-fed infants.

Tables 22 and 23 were obtained when case infants were grouped according to primary hospital diagnosis and the etiology of their illness. There was no major difference between breast-fed and formula-fed infants in percentages of meningitis, abscess or respiratory illness. Three times as many formula-fed infants had an illness involving the gastrointestinal tract (diarrhea, or vomiting and diarrhea). The largest difference between the two groups was in the "rule out sepsis" category, which is a non-specific diagnosis.

There were no substantial differences between breast-fed and formula-fed infants in the etiology of their illnesses.

Among the six infants with definite bacterial illness were four totally formula-fed babies whose illnesses were 1) staphylococcal cellulitis, 2) Salmonella diarrhea, 3) E. coli meningitis, and 4) impetigo. A fifth infant was totally breast-fed for one month, and entirely formula-fed after 1½ months of age; he was admitted with an E. coli urinary tract infection at three months of age. The sixth baby with definite bacterial illness had a Staphylococcus aureus breast abscess and was totally breast-fed at the time of admission.

Table 1

Matching Variables

		Case	(n=92)	Control	(n=92)	p
Sex	Male	69.6	(64)*	68.5	(63)	
	Female	30.4	(28)	31.5	(29)	NS
Race	Black	42.4	(39)	41.3	(38)	
	White	44.6	(41)	46.7	(43)	
	Hispanic	13.0	(12)	12.0	(11)	NS
Billing Method	Title XIX	54.3	(50)	52.2	(48)	
	Non-Title XIX	45.7	(42)	47.8	(44)	NS
Site of Health Care	Clinic	53.3	(49)	53.3	(49)	
	Private	46.7	(43)	46.7	(43)	NS

*First number represents percentage of total group of cases or controls. Number in parentheses represents the number of infants in the category.

Table 2

Other Variables

Variables		Case	(n=92)	Control	(n=92)	p
Marital Status at Birth	Single	42.4	(39)	55.4	(51)	
	Married	52.2	(48)	43.5	(40)	
	Other	5.4	(5)	1.1	(1)	.081
Gravida	1	31.5	(29)	37.0	(34)	
	2	25.0	(23)	35.2	(32)	
	3-10	43.5	(40)	27.5	(25)	.070
Para	0	35.9	(33)	46.7	(43)	
	Previous Child	63.7	(58)	53.3	(49)	NS
Type of Birth	Spontaneous Vaginal	75.0	(69)	76.1	(70)	
	Difficult Vaginal	7.6	(7)	12.0	(11)	
	Caesarean Section	16.3	(15)	12.0	(11)	NS
One-minute Apgars	Low (0-6)	9.9	(9)	7.6	(7)	
	Normal (7-10)	90.1	(82)	92.4	(85)	NS
Five-minute Rpgars	Low (0-6)	1.1	(1)	1.1	(1)	
	Normal (7-10)	98.9	(90)	98.9	(91)	NS
Neonatal Separation	None	82.6	(76)	83.7	(77)	
	Newborn Special Care Unit	17.4	(16)	16.3	(15)	NS
Mother's Age	$\leq$ 19 Years	22.0	(20)	28.9	(26)	
	20-30 Years	70.3	(64)	54.4	(49)	
	$\geq$ 31 Years	7.7	(7)	16.7	(15)	.059
Telephone Interview	Clinic Patient (no interview done)	53.3	(49)	53.3	(49)	
	Complete	37.0	(34)	43.5	(40)	
	Refused	2.2	(2)	0		
	Not Reached	7.6	(7)	3.3	(3)	NS

Table 3

Mode of Feeding at Postpartum Discharge and on Admission or Comparable Age

	Mode of Feeding	Case (n=92)		Control (n=92)		p
Feeding at Discharge	Formula	72.8	(67)	68.5	(63)	
	Breast	27.2	(25)	31.5	(29)	>.5
Feeding on Admission	Formula	87.7	(77)	70.7	(65)	
	Breast Only	14.1	(13)	25.0	(23)	
	Breast Plus Solids	1.1	(1)	3.3	(3)	
	Breast Plus Formula	1.1	(1)	1.1	(1)	.188

Table 4

Mode of Feeding on Admission or Comparable Age

All Breast-Fed Infants Grouped Together

Mode of Feeding	Case (n=92)	Control (n=92)	p
Formula	83.7 (77)	70.7 (65)	
Breast	16.3 (15)	29.3 (27)	.036

Table 5

Mode of Feeding. Stratification by Method of Payment

Mode of Feeding	Non-Title XIX				Title XIX			
	Case (n=92)		Control (n=44)		Case (n=50)		Control (n=48)	
Feeding at Discharge:								
Formula	57.1	(24)	43.2	(19)	86.0	(43)	91.7	(44)
Breast	42.9	(18)	56.8	(25)	14.0	(7)	8.3	(4)
				NS				NS
Feeding on Admission:								
Formula	71.4	(30)	47.7	(21)	94.0	(47)	91.7	(44)
Breast	26.2	(11)	45.5	(20)	4.0	(2)	6.3	(3)
Breast and Solids	2.4	(1)	6.8	(3)	0		0	
Breast plus Formula	0		0		2.0	(1)	2.1	(1)
				p=.077				NS

Table 6

Mode of Feeding at Age of Admission, All Breast-Fed Infants Grouped. Stratification by Method of Payment

	Non-Title XIX		Title XIX	
Mode of Feeding	Case (n=42)	Control (n=44)	Case (n=50)	Control (n=48)
Formula	71.4 (30)	47.7 (21)	94.0 (47)	91.7 (44)
Breast	28.6 (12)	52.3 (23)	6.0 (3)	8.3 (4)
		p = .026		NS

Table 7

Mode of Feeding. Comparison of Total Private Doctor Sample with Telephone Interview Sample

Feeding at Discharge:

	Total Private Sample		Interview Sample	
Mode of Feeding	Case (n=43)	Control (n=43)	Case (n=34)	Control (n=40)
Formula	55.8 (24)	41.9 (18)	52.9 (18)	37.5 (15)
Breast	44.2 (19)	58.1 (25)	47.1 (16)	62.5 (25)
		p = .196		p = .183

Feeding on Admission:

	Total Private Sample		Interview Sample	
Mode of Feeding	Case (n=43)	Control (n=43)	Case (n=34)	Control (n=40)
Formula	69.8 (30)	46.5 (20)	67.6 (23)	42.5 (17)
Breast	30.2 (13)	53.5 (23)	32.4 (11)	57.5 (23)
		p = .029		p = .031

Table 8

Social-Demographic Data. Interview Population

Variable		Case (n=34)		Control (n=40)		p
Mother's Education	At Least One Year of College	50.0	(17)	67.5	(27)	
	High School Grad or Less	50.0	(17)	32.5	(13)	
						NS
Father's Education	At Least One Year of College	44.1	(15)	60.0	(24)	
	High School Grad or Less	55.9	(19)	40.0	(16)	
						NS
Mother's Work	Hollingshead 1, 2, 3	32.3	(11)	42.5	(17)	
	Hollingshead 4, 5, 6, 7	64.7	(22)	57.5	(23)	
						NS
Father's Work	Hollingshead 1, 2, 3	41.2	(14)	50.0	(20)	
	Hollingshead 4, 5, 6, 7	58.8	(20)	50.0	(20)	
						NS
SES	Classes I and II	26.5	(9)	37.5	(15)	
	Classes III, IV, V	73.5	(25)	62.5	(25)	
						.313

Table 9

Health Behaviors Showing Significant Differences Between Cases and Controls

Health Behavior		Case (n=34)		Control (n=40)		p
1. Smoking in Household at Age of Admission	No	23.5	(8)	62.5	(25)	
	Yes	76.5	(26)	37.5	(15)	< .001
Mother Smoking	No	67.6	(23)	72.5	(29)	
	< 1 PPD*	11.8	(4)	12.5	(5)	
	≥ 1 PPD	20.6	(7)	15.0	(6)	NS
Father Smoking	No	41.2	(14)	67.5	(27)	
	< 1 PPD	5.9	(2)	12.5	(5)	
	≥ 1 PPD	44.1	(15)	17.5	(7)	.057
2. Limitation of Salt Intake	No	38.2	(13)	35.0	(14	
	Sometimes	14.7	(5)	0		
	Usually	23.5	(8)	20.0	(8)	
	Always	23.5	(8)	45.0	(18)	.038
3. Refined Sugar Intake Per Week	None	5.9	(2)			
	1-7 Times	79.4	(27)	100.0	(40)	
	> 7 Times	14.7	(5)			.011

*PPD = pack per day.

Table 10

Health Indices

Health Index		Case (n=34)		Control (n=40)		p
Child Health Index	Low (0-9)	61.8	(21)	38.5	(15)	
	High (10-15)	38.2	(13)	61.5	(24)	.047
Maternal Health Index	Low (0-9)	58.8	(20)	37.5	(15)	
	High (10-17)	41.2	(14)	62.5	(25)	.068

Table 11

Admission Feeding and Social-Demographic Data

Social-Demographic Variable		Formula (n=40)		Breast (n=34)	
Mother's Educational Category	High	40.0	(16)	82.4	(28)
	Low	60.0	(24)	17.6	(6)
Father's Educational Category	High	35.0	(14)	73.5	(25)
	Low	65.0	(26)	26.5	(9)
SES	High	12.5	(5)	55.9	(19)
	Low	87.5	(35)	44.1	(15)

Table 12

Social Class I: Feeding on Admission

Mode of Feeding	Case (n=4)	Control (n=9)
Formula	50.0 (2)	
Breast	50.0 (2)	100.0 (9)
		p = .022

Table 13

Stratification by SES: Mode of Feeding on Admission

High SES (I, II)

Mode of Feeding	Case (n=9)		Control (n=15)		p
Formula	44.4	(4)	6.7	(1)	
Breast	55.6	(5)	93.3	(14)	.028

Low SES (III, IV, V)

Mode of Feeding	Case (n=25)		Control (n=25)		p
Formula	76.0	(19)	64.0	(16)	
Breast	24.0	(6)	36.0	(9)	.354

Table 14

Maternal Smoking and Feeding on Admission

Maternal Smoking	Formula (n=40)		Breast (n=34)	
None	57.5	(23)	85.3	(29)
< 1 PPD	12.5	(5)	11.8	(4)
≥ 1 PPD	30.0	(12)	2.9	(1)

Table 15

Smoking in Household and Feeding on Admission

No Smoking:

Mode of Feeding	Case (n=8)		Control (n=25)	
Formula	50.0	(4)	36.0	(9)
Breast	50.0	(4)	64.0	(16)

Smoking:

Mode of Feeding	Case (n=26)		Control (n=15)	
Formula	73.1	(19)	53.3	(8)
Breast	26.9	(7)	46.7	(7)

Table 16

Child Health Index Stratification. Feeding on Admission

CHI Score	Mode of Feeding	Case (n=34)		Control (n=39)		
Low CHI	Formula	71.4	(15)	66.7	(10)	
	Breast	28.6	(6)	33.3	(5)	
						p=NS
High CHI	Formula	61.5	(8)	29.2	(7)	
	Breast	38.5	(5)	70.8	(17)	
						p=< .05

Table 17

Maternal Health Index Stratification.

Feeding on Admission

MHI Score	Mode of Feeding	Case (n=34)		Control (n=40)		
Low MHI	Formula	60.0	(12)	66.7	(10)	
	Breast	40.0	(8)	33.3	(5)	
						NS
High MHI	Formula	78.6	(11)	28.0	(7)	
	Breast	21.4	(3)	72.0	(18)	
						<.01

Table 18

Maternal Smoking and Maternal Education

	Maternal Education Category	
Maternal Smoking	High (n=44)	Low (n=30)
None	81.8 (36)	53.3 (16)
< 1 PPD	13.6 (6)	10.0 (3)
≥ 1 PPD	4.5 (2)	36.7 (11)

Table 19

Smoking in Household and SES

	SES Category	
Smoking	High	Low
No	75.0 (18)	30.0 (15)
Yes	25.0 (6)	70.0 (35)

Table 20

Stratification by SES: Child Health Index

High SES

CHI Score	Case (n=9)	Control (n=15)	
Low CHI	33.3 (3)	13.3 (2)	
High CHI	66.7 (6)	86.7 (13)	
			NS

Low SES

CHI Score	Case (n=25)	Control (n=24)	
Low CHI	72.0 (18)	54.2 (13)	
High CHI	28.0 (7)	45.8 (11)	
			NS

Table 21

Stratification by SES: Maternal Health Index

High SES

MHI Score	Case (n=9)		Control (n=15)		
Low MHI	77.8	(7)	13.3	(2)	
High MHI	22.2	(2)	86.7	(13)	
					p=.003

Low SES

MHI Score	Case (n=25)		Control (n=25)		
Low MHI	52.0	(13)	52.0	(13)	
High MHI	48.0	(12)	48.0	(12)	
					NS

Table 22

Mode of Feeding on Admission and Hospital Diagnosis in Cases

Diagnosis	Formula (n=77)		Breast (n=15)	
Rule Out Sepsis	26.0	(20)	53.3	(8)
Sepsis	0		0	
Meningitis	18.2	(14)*	13.3	(2)**
Diarrhea	15.6	(12)	6.7	(1)
Vomiting and Diarrhea	3.9	(3)	0	
Abscess	0		6.7	(1)
Respiratory	20.8	(16)	13.3	(2)
Other	15.6	(12)	6.7	(1)

* 1 case was bacterial (E. coli); 13 were viral.

** Both cases were viral.

Table 23

Mode of Feeding on Admission and Etiology in Cases

Etiology	Formula	Breast
Definite bacterial	6.5 (5)	6.7 (1)
Definite viral	10.4 (8)	13.3 (2)
Probable bacterial	2.6 (2)	0
Probable viral	51.9 (40)	60.0 (9)
Cannot assign	28.6 (22)	20.0 (3)

DISCUSSION

1. Methods

a) Case-Control Design

Horwitz and Feinstein's methodological standards for case-control research were applied as rigorously as possible in the design and performance of this study.

A predetermined method of patient selection was employed, and the protective agent, breast-feeding, was clearly defined. A matched control group was provided. Data collection was as unbiased as possible when a chart review is done by the principal investigator. There was no effort to provide anamnestic equivalence for those cases and controls whose feeding data had to be gathered by telephone interview, nor was the feeding data obtained by interview compared with the private pediatrician's office record. These weaknesses, however, are unlikely to seriously affect the results. In general, the addition of solids or formula to a breast-fed infant's diet or termination of breast-feeding was often related to a specific event, and mothers appeared to remember it clearly. Equal pre-hospitalization surveillance was achieved by taking case-control pairs from the same practice or from a clinic setting.

b) Telephone Interview

Of note in studying the results of the telephone interview is the small number of cases (34) and controls (40) actually under

consideration. In addition, there are a number of other difficulties to be kept in mind when the results of the interview data analysis are examined:

(1) While these two interviewed groups reflected the make-up of the larger private-doctor group in terms of mode of feeding, there were more upper SES families among the interviewed controls than among the interviewed cases, which might influence the risk of illness.

(2) It was not possible to blind the interviewers, as they needed to have a name by which to identify and address the person to be interviewed; because the interviewers had done the chart review for cases and controls, they knew the names of families in each group. In addition, the interviewers had first names for the case infants and only "BB" and "BG" to preface the surname for control infants.

(3) Several of the questions about health behavior were culturally biased. People with lower SES would be less likely to use a baby carrier or car seat, or to obtain regular dental care because of expense; they are more likely to be overweight.

2. Results

No significant differences in matching variables and other important variables which might have biased the findings were found between cases and controls in the study sample. When the entire

study sample was analyzed, the results indicate that breast-feeding is protective against illness serious enough to require hospitalization in the first three months of life. At the time of discharge from the post-partum ward, there was no significant difference between cases and controls in mode of feeding. However, by the age of admission, significantly more control infants were breast-fed. This indicates that more initially breast-fed case infants had been switched to formula. The difference between cases and controls was not noted in the Title XIX clinic population; however, in this group, exposure to the protective factor, breast-feeding, was not high enough for definitive conclusions to be reached.

The differences in the over all population were due to differences in the non-Title XIX private physician group. In these patients, significantly more controls were breast-fed at age of admission. Further examination of the patients of private doctors revealed that breast-feeding was protective only in the upper social class group, particularly in class I.

When each individual health attitude or behavior was compared between interviewed subjects, differences were observed in only three variables. More controls than cases had healthy behaviors: no smoking, limited salt intake and limited intake of refined sugar. Assembly of the individual attitudes and behaviors into two health indices related to child health behavior and maternal health behavior

revealed differences between cases and controls: more controls scored well on these indices ($p = .047$ for the CHI and $p = .068$ for the MHI). Controls in general appeared to have a greater awareness of what constituted appropriate care-taking for their infants and for themselves.

Of note, however, is the heavy weighting of smoking behavior in the CHI: 4 points were given (of a possible total of 15) for no smoking in the household at age of interest, 1 point was given if only the father smoked (on the presumption of less contact per day with the infant), and no points were given if the mother smoked, regardless of amount. Because of the heavy weighting of smoking, it was not surprising that more non-smokers had a high CHI. Since there were more non-smokers in the controls, differences in the CHI between cases and controls were likely to be due partially to smoking behavior.

In the MHI, where smoking was not as dramatically weighted ("no smoking at interview" was given 2 points of a possible total of 17), more controls again had a high MHI, though the difference did not reach statistical significant ($p = .068$).

When the interview population was stratified by SES, in the presence of low SES, maternal health attitudes and behaviors did not affect morbidity. However, in the presence of high SES, a high MHI (but not a high CHI) offered protection.

The precise role of smoking is difficult to determine. Non-smoking was associated with breast-feeding, high parental educational status (with high maternal education being particularly striking), high SES, high CHI and high MHI. However, while significantly more control households contained no smokers, breast-feeding per se offered no protective advantage to infants in either non-smoking or smoking households.

In summary, this study found sub-groups in which breast-feeding was protective: the non-Title XIX/private doctor population, particularly those families with high SES and high health awareness. These results are very different from previous studies: see the comparative section below for further discussion.

In spite of the complex relationships between breast-feeding, SES, smoking, and health behavior, it can be said that breast-feeding cannot override the detrimental effects of the environment associated with low SES and low maternal health awareness. However, in the presence of high SES and high maternal health behavior, breast-feeding is advantageous.

Previous studies have shown that breast-feeding is protective in developing countries. In industrialized countries, several studies have shown that breast-feeding protects in all social strata. The present study's findings are quire different. One hypothesis to explain the difference is that breast-feeding pays off in circumstances in which there are no major stresses in the infant's life.

3. Comparison With the Literature

This study agrees in part with the finding of many studies that breast-feeding protects against infectious illness. In the study reported here, the protective effect of breast-feeding can be seen only in the higher socioeconomic group. In contrast, Cunningham demonstrated benefit for breast-fed infants independent of lower educational level, a component of SES.

The study by Fallot et al is the most relevant for comparison to the present study because of its focus on hospitalized infants. The present study went beyond the Fallot study in providing matched controls and in its use of stratifications. Nevertheless, there are some similarities in the findings. Both studies show a small number of breast-fed clinic infants. In Fallot's clinic population, when well infants (14.9%) and hospitalized infants (11.3%) who are totally or partially breast-fed are compared, the percentages are quite similar. Therefore, the protective advantage claimed for breast-feeding in the Fallot study really resided in the private patients, 40.7% of whom were breast-fed among well infants, compared to 16.9% of hospitalized infants. This is strikingly similar to results noted in the present paper: in the non-Title XIX population, 52.3% of controls were breast-fed compared to 28.6% of cases. In the Fallot study 23.8% more well infants are breast-fed, and 23.7% more controls are breast-fed in this study.

In contrast to the Fallot study's finding of no proven bacterial infections in exclusively breast-fed infants, in this study the percentages of breast-fed and non-breast-fed infants with proven bacterial illnesses were identical. In the present study, as in that of Fallot and others, there was more gastrointestinal illness in formula-fed infants. The reduction in respiratory disease found in the work of Fallot, Chandra, etc., was not noted in this study; however, the number of infants in each diagnostic category is small.

4. Implications. Suggestions for Future Work.

A carefully designed study confirms in part the general finding of the literature that breast-feeding is protective against serious illness. However, this protection was demonstrated to exist only for a small group of families, those with high SES and associated high maternal health behavior. From the results of this study, it would appear that breast-feeding in very young children may not be as protective as indicated by previous investigators. However, further work needs to be done to clarify this finding. It would be particularly important to try to increase the number of breast-fed clinic infants in the study.

In the present study, it was difficult to sort out with certainty the interrelationships of breast-feeding, SES, smoking and health behavior. The small number of cases and controls interviewd prevented the reliable use of more definitive statistical techniques to delineate

the influence of each variable on the risk of hospitalization in the first three months of life.

To provide further clarification, two efforts would be appropriate:

1) Extend the present study in order to accumulate a larger number of interviewed families, so that statistical analysis might clarify the relationship between the presumed protective factor and other variables.

2) Perform a longitudinal cohort study involving a large number of infants, since hospitalization is a rare event in infancy. This type of study, though expensive and time-consuming, would facilitate clarification of the relationship between breast-feeding and all types of illness, both mild and severe, and the influence of other factors such as smoking, health consciousness, and SES on the risk of hospitalization.

Even if breast-feeding *per se* is not found to be protective against hospitalization for young infants, good reasons for breast-feeding exist in the spheres of psychology, immunology and nutrition, and health care givers can continue to use these data to encourage mothers interested in breast-feeding.

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APPENDIX

Yale University *New Haven, Connecticut 06510*

SCHOOL OF MEDICINE
333 Cedar Street
Department of Pediatrics
Telephone _____

December 8, 1980

Dear

For the thesis that is part of my work as a fourth year Yale medical student, I am conducting a case-control study that will examine the relationship between mode of feeding and hospitalizations during the first three months of a child's life. I want to describe for you the purposes of my study because a portion of it will involve interviewing by telephone parents of children who are cases and controls, some of whom may be your patients. If you do not want me (or Donna Torcia, my thesis adviser's research assistant) to interview the parents of your patients, please let me know as soon as you have read this letter, and your patients will not be included in the interview portion of my study. This study has been approved by Dr. Howard Pearson and by the Medical School's Human Investigation Committee.

As you know, studies have indicated that breastfeeding of the very young infant offers protection against illness, particularly due to infectious processes. A careful reading of many of these studies, however, reveals methodological problems (for example, lack of appropriate controls and failure to consider important variables) or numbers too small for statistical significance, particularly in those studies examining hospitalization. My study is designed to eliminate these methodological problems and to provide sufficient numbers of case-control pairs so that our conclusions will be statistically valid.

I am studying all infants less than three months old, discharged from Yale-New Haven Hospital between January 1, 1979 and June 30, 1980 who meet the following criteria:

1) born at Yale-New Haven Hospital
2) discharged with the mother as a neonate
3) without a congenital anomaly that would directly affect mode of feeding
4) admitted for: a) an infectious or suspected infectious disease, or b) non-infectious processes such as near-miss SIDS or pyloric stenosis.

I will obtain for each case a control infant matched for date of birth, sex, race, method of billing (as a rough indicator of socioeconomic status) and site of pediatric care (to attempt to decrease community differences and bias introduced by physician threshhold for hospital admission). I will then look at the number of breastfed children in each group.

To collect data on the cases and controls, we will be conducting 10-15 minute telephone interviews with the mothers with the following purposes:

1) to review or provide information about the child's feeding in the first three months.
2) to provide better measures of socioeconomic status, including parental education and employment.
3) to delineate variables that may be related to infectious processes, such as the number and ages of siblings and other people in the home, regular participation in day care, or baby-sitting arrangements.
4) to provide information about the family's attitudes toward safety and health care.

This information will be obtained so that we can attempt to isolate the effect of breastfeeding from the effects of such variables as contact with other young children or parental attitudes and behaviors.

We hope to generate conclusions that will be useful to all health care providers, and we intend to make our conclusions available to you and the medical community at large.

At this point, we wanted to make you aware of the study and to ask for your cooperation. In a small percentage of subjects, we will be asking the mothers for permission to review feeding histories in the pediatric office charts. We would like to ask your cooperation with this, should we need to consult your records.

Enclosed is a copy of the release form to be signed by parents and a copy of the questions to be asked during the telephone interview. If you wish more information or have any questions or objections, please call me (Cynthia Aten) in the evenings at 436-8211.

Sincerely,

Cynthia B. Aten
Yale Medical Student IV

John M. Leventhal, M.D.
Faculty Adviser
Assistant Professor of Pediatrics

CBA:amk

December 8, 1980

Dear

We are on the Pediatric staff at Yale-New Haven Hospital and are writing to invite you to participate in a study we are conducting. This study is about the relationship between early infant feeding and hospitalization of babies during the first few months of life. The Department of Pediatrics is cooperating with us in this study and has given us permission to contact families of children who were hospitalized at Yale-New Haven Hospital during their first three months of life in 1979 or 1980.

As part of this study, we are interested in learning about who is in your family, how you fed your infant and whether there were any illnesses in your family when your child was a baby. We would also like to find out about your views on health related behaviors (such as how your child travels in a car). In addition, we would ask your permission to review your pediatrician's records for your child's feeding history (please see the attached form).

In the next two weeks, Donna Torcia, a research assistant, or Cynthia Aten will be calling to see whether you would like to participate in this study. If you agree and the timing is convenient for you, we would like to interview you on the phone for approximately 10-15 minutes. If you would rather not participate, you can refuse by telling us at the time of the phone call. If you agree to participate, you are free to refuse to answer any particular question. You and your child may not benefit directly from our study, but we expect our findings to be useful to health care workers discussing infant feeding with parents-to-be.

We hope that you will be interested in participating in this study. If you decide not to participate, your refusal will in no way affect the care you or your child receives at Yale-New Haven Hospital or your relationship with your own personal physician, the Yale-New Haven Medical Center, or its staff.

Thank you for your consideration of our invitation.

Sincerely,

Cynthia B. Aten, Fourth Year Student,
Yale School of Medicine

John M. Leventhal, M.D.
Assistant Professor of Pediatrics

Yale University *New Haven, Connecticut 06510*

SCHOOL OF MEDICINE
333 Cedar Street

Department of Pediatrics
Telephone _____

Dear

We are on the Pediatric staff at Yale-New Haven Hospital and are writing to invite you to participate in a study we are conducting. This study is about the relationship between early infant feeding and hospitalization of babies during the first few months of life. The Department of Pediatrics at the Yale-New Haven Hospital is cooperating with us in this study and has given us permission to contact families of children who were born at the Memorial Unit in 1979 or 1980. We have chosen your child's name from the birth records to help us establish a group of children who were not admitted to the hospital between one week and three months of age.

As part of this study, we are interested in learning about who is in your family, how you fed your infant and whether there were any illnesses in your family when your child was a baby. We would also like to find out about your views on safety and health care (such as how your child travels in a car). In addition, we would ask your permission to review your pediatrician's records for your child's feeding history (please see the attached form).

In the next two weeks, Donna Torcia, a research assistant, or Cynthia Aten will be calling to see whether you would like to participate in this study. If you agree and the timing is convenient for you, we would like to interview you on the phone for approximately 10-15 minutes. If you would rather not participate, you can refuse by telling us at the time of the phone call. If you agree to participate, you are free to refuse to answer any particular question. You and your child may not benefit directly from our study, but we expect our findings to be useful to health care workers discussing infant feeding with parents-to-be.

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Thank you for your consideration of our invitation.

Sincerely,

Cynthia B. Aten, Fourth Year Student,
Yale School of Medicine

John M. Leventhal, M.D.
Assistant Professor of Pediatrics

Case #

Data Abstraction Sheet
Case/Control Study of Breastfeeding
and Hospitalization 10/31/80

ID #

Date of admission
Age of admission

Diagnosis, pertinent facts

Date of Birth _____

Sex _____

Race _____

Billing Method

_____

Site of Health Care

_____

Feeding history: birth
interim
on admission

Mother: Date of birth, age
Marital status
Parity
Significant facts about
this pregnancy

Infant: Birth: mode of birth
weight
gestational age
Apgars

Neonatal:

Telephone Interview Schedule

Child's current age _____
Age of interest: birth to _____
Child's first name _____
No. _____
Date of interview _____

Establish identity of person who who answers.
This is Donna Torcia from the Pediatrics Department of Yale-New Haven Hospital.

Did you receive Cynthia Aten's letter about the study concerning how babies are fed and hospitalization in the 1st 3 months of life?
Yes ____ No ____

Participation in the study would involve my talking with you for about 10-15 minutes by telephone. It would not be necessary for you or _____ to be seen. All information is confidential.

Would you be willing to participate? Is this a good time for you?
Yes ____ No ____

During the interview I'll be asking questions about a variety of topics having to do with you and your family. You are free to choose not to answer any particular question. Please feel free to ask me to repeat a question if you don't understand it. Any questions so far?

I am particularly interested in talking about your child who is now _____. What do you call him/her? _____

I. Feeding

To begin, I would like to ask you some questions about how you fed _____ as a young infant. I'm especially interested in his/her first _____ of life.

1) Had you decided how you would feed _____ before s/he was born? Yes ___ No ___

2) What were the things you thought about as you decided?

3) Did anything happen to change your plans for feeding? If yes, what was it? Yes ___ No ___

4) Did you attend childbirth classes before _____ was born? What was your reason for this? Yes ___ No ___

5) How did you feed _____ just after birth, in the hospital?
Breast _____
Formula _____
Both _____

If breast-fed:
How long did you breast-feed _____?

If formula-fed:
How long did you continue bottle feeding? _____

When did you first introduce
something other than breast milk?

_____ _____

How often was s/he taking this?

_____

Classification: ___ exclusively breast-fed
___ breast-fed plus _____
when added _____
___ switched
when switched _____
___ exclusively formula-fed

II. Demographic/SES

Now I'd like to ask you a few questions about you and your household.

1) Are you married?

Single _____
Married _____
Separated _____
Divorced _____
Other _____

2) How far have you gone with your education?

3) How far has _____'s father gone with his education?

4) What sort of work do you do, or have you done?

5) What sort of work does _____'s father do?

SES Classification _____

I'd like to ask you what your household was like when _____ was _____ old. (age of interest)

6) Who was living with you and _____ during his/her first _____?
(age of interest)

If any children:

7) What were the approximate ages of the children in the household at this time? _____

8) Were there any infectious illnesses (such as colds, "flu") in your household during this time? Yes ___ No __ Don't Recall ___

9) Was _____ in contact with other children through day care or a babysitting arrangement during this time? Yes ___ No ___

If yes, what were the approximate ages of these children? _____

For controls:

10) Was _____ sick at all during her/his _____? Yes ___ No ___

If yes: did you go to the doctor for this? Yes ___ No ___ Called ___

III. Health Behaviors/ Attitudes

Now I'd like to ask you some questions about how things are done in your family.

1) Does anyone in hour household smoke? Yes ___ No ___

If yes: Who, and how much? _____

Did this person smoke when _____ was _____(age of interest)? Yes ___ No ___

Ask only if child now more than 10 months old:

2) Do you have ipecac at home: Yes ___ No ___

If don't know: (a medicine to make a child vomit up a poison).

If yes: Have you had to use it? Yes ___ No ___

Why? _____

3) Has _____ missed any appointments for regular check-ups in the past year? Yes ___ No ___

If yes: Was the appointment rescheduled and kept? Yes ___ No ___

4) Is _____ up to date on his/her baby shots? Yes ___ No ___

5) Did you use any sort of baby carrier, like a Snuggli, when _____ was a small baby? Yes ___ No ___

6) Do you use a restraint system for _____ when s/he travels in a car? Yes ___ No ___

If yes: How often? Always _____
Usually _____
Sometimes _____

What kind? _____

7) Have you made a trip greater than 1 mile in a car in the past day? Yes ___ No ___

If yes: Did you use a seat belt? Yes ___ No ___

If no: When was the last time you were in a car? _____

Did you use a seat belt at this time? Yes ___ No ___

8) When was the last time you saw a dentist? _____

9) When was the last time you had a Pap smear? _____

10) Within the last 2 years, when you were not pregnant, have you been told by your doctor that you were overweight? Yes ___ No ___

11) Do you try to limit the amount of salt you eat? Yes ___ No ___

If yes: How consistently? Always _____
Sometimes _____
Usually _____

12) How many soft drinks did you drink this past week? _____

13) How many cups of coffee or tea did you have yesterday? _____
Was that a typical day in terms of your intake? Yes ___ No ___
If no: Do you usually drink more or less? More __ Less __

14) How many times this past week did your family eat a sweet dessert or between-meal snack? _____

15) Over the last month, have you taken any sort of regular exercise? Yes____ No ___

If yes: What? _____
How often? _____
For how long? _____

16) Within the last week, have you experienced a stressful period (feeling uptight, anxious, nervous)? Yes ___ No ___

If yes: What did you find helpful in coping with this stress? _____

These are all the questions I have for you. Do you have any questions for me? Thank you very much for your cooperation this morning/afternoon. We certainly do appreciate your being willing to answer our questions and share so much helpful information with us.

Child Health Index

1)	Deciding how to feed (#6)	No = 0 Yes = 1	1) _____
2)	Prenatal classes (#9)	No = 0 Yes or previous classes = 1	2 _____
3)	Smoking during age of interest	No = 4 Father = 1 Mother = 0	3 _____
4)	Ipecac in house	No = 0 Yes but used = 1 Yes = 2 or child less than 10 months old	4) _____
5)	Check-ups	None missed or reschedule = 1 Missed appt. = 0	5) _____
6)	Immunizations up to date	Yes = 1 No = 0	6) _____
7)	Appropriate car restraint	Yes, always=4 Yes, usually=2 Yes, sometimes=1 No =0	7) _____
8)	Baby carrier	Yes = 1 No = 0	8) _____

Range = 0-15

Total _____

Maternal Health Index

1)	Smoking at time of interview	No = 2 Yes = 0	1) _____
2)	Seat belt	Yes = 2 No = 0	2) _____
3)	Dentist	$\geq$ 1 year = 0 $<$ 1 year = 1	3) _____
4)	Pap smear	$>$ 1½ year = 0 $<$ 1½ year = 1	4) _____
5)	Weight	yes, overweight = 0 no = 1	5) _____
6)	Salt	always or usually = 2 sometimes = 1 no = 0	6) _____
7)	Soft drinks/week	$\leq$ 2-8oz. glasses = 1 $>$ 2-8oz. glasses = 0	7) _____
8)	Sweet dessert/week	$\leq$ 3/week = 2 $>$ 3 $<$ 7 = 1 $>$ 7 = 0	8) _____
9)	Caffeine (tea/coffee)/day	$\leq$ 2 cups = 2 $>$ 2 cups = 0	9) _____
10)	Exercise	none = 0 $\leq$ 2 times/week calisthenics = 1 >2 times/week calisthenics or aerobic $\leq$ 2 times/week=2 aerobic $>$ 3 times/week=3	10) _____

Range 0-17 Total _____

Coding Criteria
Card 1

1. Card #1

2-4. ID #

5. Case/control status
   1=case
   2=control

6. Sex
   1=M
   2=F

7. Race
   1=W
   2=B
   3=H
   4=Other (coding according to mother)

8. Billing
   1=non-T19
   2=T19
   3=unknown

9. Health care provider
   1=private
   2=clinic

10,11. Child's age in days (date of birth to date of admission) (Age of interest)

12, 13. Month of birth

14. Year of birth
   1=1979
   2=1980
   3=1981

15. Diagnosis
   0=control patient
   1=fever or rule out sepsis
   2=sepsis
   3=meningitis
   4=diarrhea, enteritis
   5=vomiting and diarrhea, gastroenteritis
   6=abscess
   7=respiratory, including otitis media
   8=other: tussive episodes associated with choking, cyanosis, hypernatremic dehydration, probable viral syndrome, r/o meningitis, staph cellulitis, impetigo, conjunctivitis.
   9=unknown

16. Etiology

0=control
1=definite bacterial (salmonella, staph, etc.) positive culture
2=definite viral (aseptic meningitis, rise in titers, viral culture positive)
3=probable bacterial, eg. chylamydia,otitis media
4=probable viral, eg. bronchiolitis, r/o sepsis with negative CX's
5=can't assign, eg. diarrhea, vomiting, pneumonia
9=unknown

17. Feeding on discharge from newborn

1=formula
2=breast
9=unknown

18. Feeding on admission
19. Feeding end of 1st month (30 days)
20. Feeding end of 2nd month (60 days)
21. Feeding end of 3rd month (90 days)

0=NA (=past age of interest)
1=formula (may include solids as well)
2=breast (may include occasional cereal or formula feed) less often than once a day
3=breast and solids (still nursing but has added solids only)
4=breast plus (nursing but has added formula; may have added solids as well)
9=unknown

22. Timing of first switch

0=no change
1=during 1st month
2=during 2nd month
3=during 3rd month
9=unknown

23. Timing of second switch

0=NA
1=during 1st month
2=during 2nd month
3=during 3rd month
9=unknown

24-25. Mother's age based on last birthday (if inknown leave blank)

9=unknown

26. Marital status at birth

1=single
2=married
3=separated
4=divorced
5=other
9=unknown

27. Gravida (code G10 as 0) — 9=unknown

28. Para — 9=unknown (not including this birth)

29. Birth
1=NSVD or low forceps
2=mid forceps or vacuum, assisted breech
3=C section
9=unknown

30-33. Birth weight in grams (if unknown leave blank)

34-35. 1 minute Apgar (if unknown leave blank)
79/193 - low Apgars, not stim because checked for meconium.

36-37. 5 minute Apgar (if unknown leave blank)

38. Neonatal separation
0=none
1=6 hour hold
2=NBSCU other than 6 hour hold
3=both
9=unknown

39. Telephone interview
0=no call because clinic patient
1=completed
2=refused
3=not reached (can't locate or moved)

Card 2

1. Card #2

2-5. As in card 1 (If no interview leave rest blank)

6. Decided how would feed
   0=no
   1=yes
   9=unknown

7. Reasons for choice
   0=no reason
   1=infant-centered (nutrition, closeness, resistance to disease, etc.)
   2=mother-centered (convenience, cost, distaste, etc.)
   (score as 1 if any valid infant-centered reasons mentioned) include back to work, mother taking drugs that didn't want in milk, eg. prednisone or doctor forbade breast-feeding because pituitary disease.
   9=unknown

8. Change of plans in newborn period
   0=no
   1=yes, medical reasons (eg. mother on antibiotics)
   2=yes, personal reasons (eg. too painful)
   3=baby not getting enough to satisfy
   4=no plans
   9=unknown

9. Childbirth classes
   0=no
   1=yes
   9=unknown

10. Reasons
   0=NA (#9=1
   1=previous classes
   2=previous birth(s) (if attended classes with previous births, score as 1)
   3=not necessary
   4=no reason
   5=other (sick, no transportation, too busy, no sitter for older child) birth date moved up 6 weeks, therefore no time.
   9=unknown

11. Length of breast feeding

0=none
1=less than 1 month
2=1-2 months
3=2-3 months
4=3-4 months
5=5-6 months
6=6-7 months
7=7-8 months
8=more than 7 months
9=unknown

12. Marital status (interview)

1=single
2=married
3=separated
4=divorced
5=other
9=unknown

13. Mother's education (according to Hollingshead)

1=graduate professional training
2=standard college or university graduate including work on MS, MSW,etc.
3=partial college training, at least 1 year
4=high school graduate
5=partial high school
6=junior high school
7=less than 7 years of school
9=unknown

14. Father's education (see 13)

15. Mother's employment (see detailed Hollingshead list) (Current or former - rank according to highest level job), include full-time students as heads of households in future employment category.

0=homemaker only
1=higher executives, proprietors of large concerns, majro professionals
2=business managers, proprietors of medium-sized businesses, lesser professionals
3=administrative personnel, small independent businesses, minor professionals
4=clerical and sales workers, technicians, owners of little businesses
5=skilled manual employees
6=machine operators and semi-skilled employees
7=unskilled employees
9=unknown

16. Father's employment (see 15).

17. SES head of household (father unless single, divorced, separated) code SES at age of interest, SES can then be computed using
7 x #15 or #16 + 4 x #13 or #14
(employment) (education)

1=I (11-17)
2=II (18-27)
3=III (28-43)
4=IV (44-60)
5=V (61-77)

children in household other than case or control (child=person less than or equal to 17 years old.)

18.	Total #	9=unknown
19.	# less than 5 years old	9=unknown
20.	# 5 years old or greater	9=unknown
21.	Infectious illness in household	0=no 1=yes 2=don't recall 9=unknown
22.	Day care/sitting	0=no 1=yes, babysitter 2=yes, group 9=unknown
23.	Ages of children in #22 If 5 years old, classed as 1	0=NA (i.e. "no" to 22) 1=most are under 5 2=most are over 5
24.	Infant sick? (for controls)	1=NA (=case) 1=no 2=yes, no doctor 3=yes, called doctor 4=yes, saw doctor 5=don't recall 9=unknown
25.	Smoke at age of interest (cigarette,not pipe)	0=no 1=yes 9=unknown

26.	Mother smoking at age of interest	0=no 1=less than 1 PPD 2=1 PPD or more 3=amount unspecified 9=unknown
27.	Smoke-father at age of interest	0=no 1=less than 1 PPD 2=1 PPD or more 3=amount unspecified or not in household 9=unknown
28.	Smoke-mother at time of interview	0=no 1=less than 1 PPD 2= 1 PPD or more 3=amount not specified 9=unknown
29.	Ipecac	0=no 1=yes 2=NA (infant now less than 10 months old) 9=unknown
30.	Had to use it?	0=no 1=yes (including use for older sib) 2=NA (either child less than 10 months or "no" to #29) 9=unknown
31.	Check-ups	0=no, has not missed <u>or</u> has made up appointments 1=yes, has missed appointment 9=unknown
32.	Immunizations up to date?	0=no 1-yes 9=unknown
33.	Baby carrier	0=no 1=yes 9=unknown
34.	Car restraint	0=no or inadequate restraint 1=sometimes 2=usually 3=always 9=unknown

35. Seat belt
0=no
1=yes
9=unknown

36. Dentist
1=less than 1 year ago
2=1 year ago or more
9=unknown

37. Pap
1=1½ years ago or less
2=more than 1½ years ago
9=unknown

38. Overweight
0=no
1=yes
2=no doctor visit
9=unknown

39. Salt (try to limit)
0=no
1=sometimes
2=usually
3=always
9=unknown

40. Soft drinks
0=none
1=2-8 oz. glasses/week or less
2=more than 2-8 oz. glasses/week
9=unknown

41. Coffee/tea - regular intake (omit decaffeinated coffee or herbal tea from count)
0=none
1=1 cup per day
2=2 cups per day
3=3 cups per day or more
9=unknown

42. Sweet dessert/snack
0=none
1=1-7
2=more than 7

43. Regular exercise - type
0=none
1=calisthenics (include exercise at home, exercise salon, tennis) less than 3 times/week
2=calisthenics 3 or more times/week
3=aerobic exercise (jogging, belly-dancing, running, swimming, cycling, aerobic dance, walking fast) less than 3 times/week
4=aerobic exercise 3 or more times/week

44. Stress and method of coping

0=no stress
1=yes - intake (eat, pot, coffee, tea, cigarette)
2=yes - solitary activity (walk, shower, lie down, meditation, write, read a book, watch TV, clean house try to get more organized, exercise, sleep)
3=yes - social activity (talk with friends or husband, visit, sex)
4=yes - avoidance activity (get out of house, away from other people)
5=yes - emotional behavior (cry, yell, scream)
6=yes - religious activity (read Bible, pray)
9=unknown (or nothing in particular)

45-46. Child health index (see separate scoring sheet).

47-48. Mother's health index (see separate scoring sheet).

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